

REMARKS / ARGUMENTS

Claims 1-6 and 10- 20 are pending. No amendments are entered by way of this response. A Listing of Claims is provided herewith for the convenience of the Examiner in consideration of this response.

35 USC § 112, first paragraph (written description)

The Examiner has rejected claims 1-6 and 20 under 35 USC § 112, first paragraph, as allegedly lacking Written Description for the use of the term "about."

Applicants respectfully disagree that Written Description is lacking for the term "about" as recited in the claims. As indicated in MPEP 2163.02, an objective standard for compliance with the written description requirement is whether *"the description clearly allow[s] persons of ordinary skill in the art to recognize that he or she invented what is claimed."* As reflecting in *In re Wertheim*, 191 USPQ 90 at 98, a 25%-60% range is understood to support a claim directed to a 35%-60% range as part of the disclosure. The burden rests on the USPTO to "give reasons why a description not in *ipsis verbis* is insufficient." *Id.*

In the present case, every range objected to by the Examiner which includes the term "about" meets the Written Description requirement consistent with MPEP 2163.02 and *In re Wertheim*. The range of about 1% to about 40% of a water soluble polymer and the range of about 5% to about 20% of polyvinylpyrrolidone are encompassed and thus supported by the 0.5% to 50% range described at page 3 of the specification. About 1% to about 8% and about 3% to about 5% of a surfactant are ranges supported by the 0.5 to 10% range at page 3. The range of about 1% to about 5% of rapamycin 42-ester with 3-hydroxy-2-(hydroxymethyl)-2-methylpropionic acid (CCI-779) is supported by the 0.5 to 25% range at page 3.

In view of the exemplary support identified within the specification, one of skill in the art would recognize, as of the filing date, that the Applicants were in

possession of the invention presently claimed as of the filing date. The Examiner has not provided any reasons why *ipsis verbis* description is required as to these ranges, in accordance with the mandate of *In re Wertheim*. Accordingly, the Examiner is respectfully requested to reconsider and withdraw this ground for rejection.

35 USC §103

That Examiner has rejected claims 1-6 and 10-20 under 35 USC § 103 as allegedly unpatentable over US Patent Application Publication No. 2002/0013335 ("Azrolan") in view of UK Patent Application No. GB 2327611 ("Haeberlin") and , Decker, 1996 ("Madhavi").

It is substantially asserted that these documents provide the components contained in Applicants' claimed compositions, and that selection of ranges of components for a composition is within the skill in the art.

Applicants respectfully request that the rejection under 35 USC § 103 be withdrawn. As stated in *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. ____ (2007), 127 S. Ct. 1727 at 1741:

“...a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art.....it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does.”

Azrolan describes methods of treating cardiovascular disease with a rapamycin which may include CCI-779. General information regarding excipients useful in formulations is provided. Haeberlin provides for stabilization of macrolides, including rapamycins generally, by formulation with an acid such as malonic acid. Madhavi describes the use of BHA and BHT in the food industry (page 277, second paragraph).

Haeberlin and Madhavi do not add anything to Azrolan which would lead one of skill in the art to the solid CCI-779 compositions presently claimed. None of these documents recognizes the problem to which the present invention is directed, *i.e.*, providing a highly bioavailable non-micronized CCI-779 formulation that avoids both

dissolution and instability problems associated with the formation of the CCI-779 compositions of the prior art by compression.

The Examiner has not provided any motivation to combine these documents to arrive at the claims presently pending. Absent the Applicants' recognition of the problem on which this invention focuses, nothing in the cited documents suggests the combination of excipients provided by the present formulation, nor could the advantages thereof be predicted. Further, it is not routine within the art to select components, which may or may not have been identified previously, and then derive a formulation of those components in order to solve the recognized problem.

The Examiner's assertion that one would combine Azrolan with Madhavi because "BHA and BHT are extensively used antioxidants," fails to supply any actual reason to combine. Similarly, that Haeberlin describes the use of acids to stabilize macrolides does not itself supply any motivation to combine with Azrolan. See *KSR Int'l Co. v. Teleflex, supra*. The Examiner has provided no reason to combine these documents, except via hindsight to reject Applicants' claimed compositions.

Even if combined, the determination of what percentage of each component to include in the composition could not be derived from these documents by one of skill in the art. Contrary to the Examiner's position at page 8, last paragraph, it is the inventive selection of components and amounts of same in order to solve the problems identified by the Applicants that yielded the presently claimed compositions.

The Examiner's arguments thus fail to provide any rationale supporting the present obviousness rejection that couldn't be equally (and improperly) applied to any new composition of elements. Accordingly, for the reasons set forth above, the Examiner is respectfully requested to reconsider and withdraw the rejection under 35 USC 103(a).

Double Patenting

Claims 1, 2-6, and 20 are provisionally rejected on the ground of non-statutory obviousness-type double patenting over claims 55, 58-61, 65 and 72-73 of copending Application No. 10/930,487 in view of Azrolan.

Applicants respectfully traverse this rejection.

Copending application 10/930,487 contains claims drawn to formulations containing amorphous CCI-779. Azrolan describes methods of treating cardiovascular disease with a rapamycin which may include CCI-779, and includes general information regarding excipients useful in formulations is provided. There is no motivation to combine Azrolan with copending application 10/930,487.

In contrast, the present application contains claims to CCI-779 with the specified excipients. Applicants believe that the claims of the two applications, in view of Azrolan, are nonobvious over the other. The Examiner's assertion that combination would be obvious to one of skill in the art provides only a legal conclusion, absent any reason for combining that could be found outside of Applicants' disclosure.

Reconsideration and withdrawal of this rejection is requested.

Claims 1, 2-6, and 20 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 7-8 and 11 of copending application no. 11/030,685 in view of Azrolan.

Copending application 11/030,658 contains claims drawn to micronized CCI-779 and formulations containing same. Azrolan describes methods of treating cardiovascular disease with a rapamycin which may include CCI-779, and includes general information regarding excipients useful in formulations is provided. There is no motivation to combine Azrolan with copending application 11/030,658.

In contrast, the present application contains claims to non-micronized CCI-779 with the specified excipients. Applicants believe that the claims of the two applications, in view of Azrolan, are nonobvious over each other. The Examiner's assertion that combination would be obvious to one of skill in the art provides only a

legal conclusion, absent any reason for combining that could be found outside of Applicants' disclosure.

Reconsideration and withdrawal of this rejection is requested.

Claims 1, 2, 4, and 6 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 12-16 and 19 of copending application no. 10/626,943.

Copending application no. 10/626,943 contains claims drawn to parenteral formulations comprising CCI-779, an alcoholic solvent, an antioxidant, a diluent solvent, and a surfactant. In contrast, the present application contains claims to compositions of CCI-779 with the specified excipients. Applicants believe that the claims of the two applications are nonobvious over each other.

The Examiner's assertion that combination would be obvious to one of skill in the art provides only a legal conclusion, absent any reason for combining that could be found outside of Applicants' disclosure.

Reconsideration and withdrawal of this rejection is requested.

In view of these remarks, Applicants respectfully request favorable consideration of the claims.

The Director is hereby authorized to charge any deficiency in any fees due with the filing of this paper or credit any overpayment in any fees to our Deposit Account Number 08-3040.

Respectfully submitted,

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